

## Case report



## Thyroid gland metastasis from breast cancer: a case report

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## Abstract

Primary cancer metastasis to thyroid gland is rare. The most common metastatic tumors of the thyroid gland are from lung, breast and renal cell carcinoma. In this case report, a patient with breast cancer metastasized to the thyroid gland is presented. A 38-year-old female patient was diagnosed with breast cancer, and positron emission tomography-computed tomography (PET-CT) imaging for breast cancer staging revealed fluoro-2deoxy-D-glucose (FDG) uptake in the thyroid nodule. Fine needle aspiration biopsy (FNAB) of the nodule revealed atypia of undetermined significance (Bethesda III). After neoadjuvant chemotherapy, simultaneous breast conserving surgery and total thyroidectomy were performed. Immunohistochemical staining of the pathological specimens revealed breast cancer that had metastasized to the thyroid gland. Immunohistochemical methods helped distinguishing primary thyroid cancer from metastasis. Also, nodules that showed activity involvement were detected randomly in PET-CT, and had to be evaluated in terms of malignancy.

## Introduction

Breast cancer is the most common cancer and the leading cause of cancer-related death in women.<sup>1</sup> Breast cancer can most commonly metastasize to the bone, lungs, pleura, liver, brain, and rarely thyroid gland.<sup>2</sup> Although thyroid gland is a highly vascularized organ, thyroid metastasis of malignant tumors is rare.<sup>3</sup> With the development of diagnostic methods in recent years, it has become possible to detect thyroid metastases earlier.<sup>4</sup> In this case report, a patient with breast cancer metastasized to thyroid gland is presented.

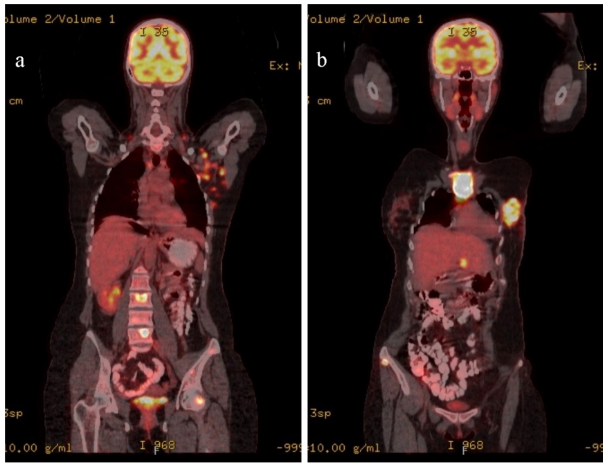
## Case Report

A 38-year-old female patient was presented with a one-year history of breast deformity. The patient did not have any known disease or positive familial history. Mammography showed a 55 mm mass on the left breast. Pectoral muscle invasion of the tumor tissue and left axillary metastatic lymphadenopathies were detected in magnetic resonance imaging (MRI). Biopsy revealed invasive breast carcinoma. Positron emission tomography-computed tomography (PET-CT) was performed for staging, and multiple metastases were detected in the lymph nodes, lungs, liver and skeletal system (Figure 1). The final diagnosis was breast carcinoma in the left breast (T4aN3M1, stage IV) with multiple metastases. Neoadjuvant docetaxel +

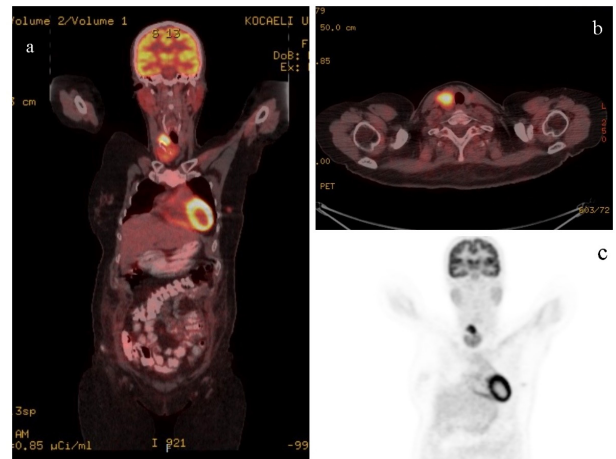
trastuzumab + bisphosphonate treatment was initiated and all metastases except the skeletal system regressed with this therapy. Treatment of the patient was maintained with trastuzumab and bisphosphonate.

At second year follow-up, a nodule showing hypermetabolic activity involvement in the right thyroid lobe was detected by PET-CT imaging (Figure 2). It was determined that the size of the heterogeneous hypoechoic nodule (TIRADS-4) in the right thyroid lobe, which was a 2-cm benign nodule as shown in previous ultrasonography (USG) and fine needle aspiration biopsy (FNAB), was doubled in control USG. Laboratory test results revealed thyroid stimulating hormone (TSH): 1.02  $\mu$ IU/mL, free T4: 0.7 ng/dL, free T3: 3.32 pg/mL, creatinine: 0.54 mg/dL, SGOT: 43.7 U/L, SGPT: 25.8 U/L, Ca: 9.1 mg/dL, Na: 142 mmol/L, K: 5.5 mmol/L, P: 4.15 mg/dL, albumin: 3.96 g/dL, and Mg: 2.3 mg/dL. FNAB was repeated because the size of the existing nodule increased and showed activity involvement in PET-CT. The cytology of the nodule was reported as atypia of undetermined significance (Bethesda III). After neoadjuvant chemotherapy, there was a shrinkage in the primary tumor focus in the left breast, and the patient underwent a modified radical mastectomy. In addition, the thyroid nodule in the category III of Bethesda, which showed enhanced tracer uptake in PET-CT, was considered to be malignant,

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**Figure 1:** Abnormal uptake areas of FDG are seen in the left axilla(a), skeletal system (a), liver(b) and left breast (b) on PET-CT imaging.

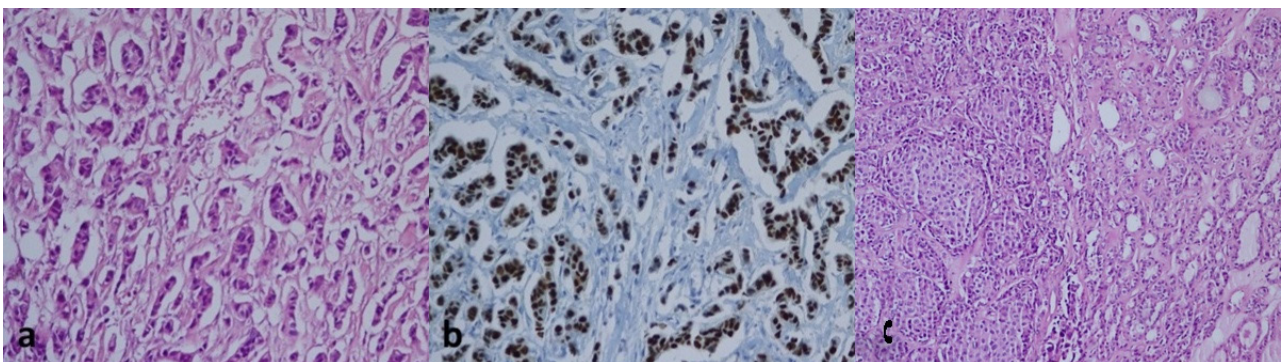


**Figure 2:** PET/CT reveals an FDG-avid focus in the right thyroid gland (a,b,c).

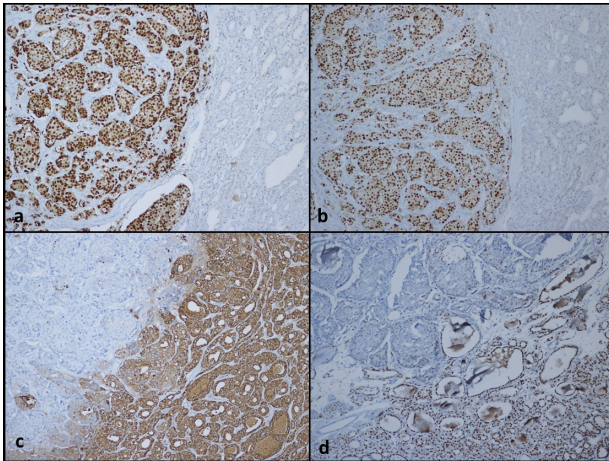
and total thyroidectomy was also performed. In the pathological evaluation, invasive breast carcinoma of no special type was detected. In immunohistochemical (IHC) evaluations, Estrogen receptor (ER) 80% strong nuclear staining, progesterone receptor (PR) 5% strong nuclear staining and CerbB2 strong membranous staining (score: 3+) were observed in tumor cells (Figure 3). Ki67 proliferation index was determined as 70%. Additionally, tumor metastasis was displayed in thyroidectomy material, in a large number of foci with a largest diameter of 12 mm (Figure 3). Also, a large number of metastatic foci with diffuse strong nuclear staining with ER and GATA-3 were detected in IHC evaluation of normal thyroid tissue, stained positively with thyroglobulin (Tg) and thyroid transcription factor-1 (TTF-1) (Figure 4). Morphological and immunohistochemical findings were evaluated as compatible with breast carcinoma metastasis. Medical treatment of the patient was maintained with trastuzumab + bifosfonat.

**Discussion**

Metastasis to the thyroid gland was first demonstrated by Virchow in 1871, describing the metastasis of the testicular tumor.<sup>5</sup> Although the thyroid gland is a highly vascular organ, it remains a rare site for metastasis. The incidence of thyroid gland metastasis varies between 1.2% and 24%.<sup>6</sup> In recent years, the number of reported cases has increased due to widespread use of FNAB.<sup>7</sup> It has been shown that more than 90% accuracy is obtained in the diagnosis of secondary tumors of the thyroid by FNAB.<sup>8</sup> The most common tumors metastasizing to thyroid gland are renal cell carcinoma, nasopharyngeal cancer, breast cancer and lung cancer.<sup>7-9</sup> Cancers with thyroid gland metastasis develop usually in women and particularly in older ages.<sup>10</sup> Similarly, our patient was a woman, but thyroid metastasis was observed at an earlier age in our patient, unlike the literature. Thyroid gland metastases are usually seen in the advanced stages of primary tumors and are associated with other



**Figure 3:** Histological features of the tumor. Hematoxylin-eosin stain revealed a invasive breast cancer of no special type (a). The tumor was ER positive for 80% of tumor cells (b). Metastatic breast cancer focus (left side) in normal thyroid tissue (right side) (c).



**Figure 4:** The tumor cells express nuclear positivity for GATA-3 (a) and ER (b) immunohistochemistry. Tg (c) and TTF-1 (d) positivity in normal thyroid tissue.

organ metastases.<sup>11</sup> In our case with thyroid gland metastasis, an advanced cancer (T4aN3M1, stage IV) was demonstrated in concordance with the literature. Thyroid metastases are often seen as metachronous. The longest period between the initial diagnosis of primary tumors and metastasis to the gland is reported to be 21 years.<sup>12</sup> However, in some studies it is mentioned that it depends on the stage of the primary tumor and the extent of the disease rather than metastasis to the thyroid gland.<sup>6</sup> In our patient, the time between the thyroid metastasis and the breast cancer diagnosis is approximately 2 years.

The diagnosis of thyroid gland metastasis is difficult because most of the patients are asymptomatic.<sup>13</sup> When treating patients with a history of malignancy, it should be kept in mind that the nodule in the thyroid gland may be a metastatic lesion, even if the diagnosis of the primary tumor has been diagnosed a long time ago.<sup>10</sup> When the nodule is detected, a FNAB helps to provide a quick and easy diagnosis.<sup>11</sup> IHC methods may help to confirm metastatic lesions of the thyroid gland on pathologic specimens. Metastatic lesions were negative for thyroglobulin and calcitonin. Since TTF-1 is positive in both thyroid and lung malignancies, the importance of that marker is not significant. Metastatic renal cell carcinomas are positive for CD10, vimentin and renal cell carcinoma antigen. ER and PR may be positive in metastatic breast carcinoma.<sup>14</sup> GATA-3 is a reliable and sensitive diagnostic marker for breast cancer metastases.<sup>15</sup> A study has shown that GATA-3 expression is closely related to ER positivity in breast cancer.<sup>16</sup> In our patient's thyroid gland, it was found that ER and GATA-3 showed strong nuclear staining, which was compatible with breast cancer metastasis.

With the help of histopathology and IHC in the reported case, metastasis of breast carcinoma to thyroid gland was confirmed. IHC methods were helpful in distinguishing metastatic breast carcinoma from primary thyroid

malignancy. Similar to the expression pattern of primary breast carcinoma, it was found that ER was positive in the metastatic tumor. GATA-3 positivity in thyroid metastasis also supported breast cancer metastasis.

In this case, it was emphasized that the shape and size changes in the thyroid nodules may be important in terms of metastasis in patients with primary malignancy, and IHC methods may be beneficial in the diagnosis. In addition, localized increased tracer activity incidentally detected in PET-CT should be evaluated by USG and FNAB if needed, in terms of possible metastasis or primary thyroid malignancy.

**Conflict of Interest**

None.

**Ethical Approval**

Not applicable.

**Authors' contributions**

All authors contributed to the obtaining of data, revised the paper and gave final approval.

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**References**

1. WHO. Breast Cancer: Prevention and Control. Geneva: WHO; 2012.
2. Irvin W Jr, Muss HB, Mayer DK. Symptom management in metastatic breast cancer. *Oncologist*. 2011;16(9):1203-14. doi: 10.1634/theoncologist.2011-0159.
3. Czech JM, Lichtor TR, Carney JA, van Heerden JA. Neoplasms metastatic to the thyroid gland. *Surg Gynecol Obstet*. 1982;155(4):503-5.
4. Cichoń S, Anielski R, Konturek A, Barczyński M, Cichoń W. Metastases to the thyroid gland: seventeen cases operated on in a single clinical center. *Langenbecks Arch Surg*. 2006;391(6):581-7. doi: 10.1007/s00423-006-0081-1.
5. Willis RA. Metastatic tumours in the thyreoid gland. *Am J Pathol*. 1931;7(3):187-208.3.
6. Papi G, Fadda G, Corsello SM, Corrado S, Rossi ED, Radighieri E, et al. Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10-year experience. *Clin Endocrinol (Oxf)*. 2007;66(4):565-71. doi: 10.1111/j.1365-2265.2007.02773.x.
7. Kim TY, Kim WB, Gong G, Hong SJ, Shong YK. Metastasis to the thyroid diagnosed by fine-needle aspiration biopsy. *Clin Endocrinol (Oxf)*. 2005;62(2):236-41. doi: 10.1111/j.1365-2265.2005.02206.x.
8. Aron M, Kapila K, Verma K. Role of fine-needle aspiration cytology in the diagnosis of secondary tumors of the thyroid--twenty years' experience. *Diagn Cytopathol*. 2006;34(3):240-5. doi: 10.1002/dc.20329.
9. Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA. Metastasis to the thyroid gland. A report of 43 cases.

- Cancer. 1997;79(3):574-8. doi: 10.1002/(sici)1097-0142(19970201)79:3<574::aid-cnrcr21>3.0.co;2-#.
10. Lam KY, Lo CY. Metastatic tumors of the thyroid gland: a study of 79 cases in Chinese patients. *Arch Pathol Lab Med*. 1998;122(1):37-41.
  11. Wood K, Vini L, Harmer C. Metastases to the thyroid gland: the Royal Marsden experience. *Eur J Surg Oncol*. 2004;30(6):583-8. doi: 10.1016/j.ejso.2004.03.012.
  12. Mattavelli F, Collini P, Pizzi N, Gervasoni C, Pennacchioli E, Mazzaferro V. Thyroid as a target of metastases. A case of foregut neuroendocrine carcinoma with multiple abdominal metastases and a thyroid localization after 21 years. *Tumori*. 2008;94(1):110-3.
  13. Lakshminarayanan M, Kurian A. A rare presentation of metastasis to the thyroid gland. *J Clin Diagn Res*. 2017;11(4):ED19-ED20. doi: 10.7860/jcdr/2017/24696.9709.
  14. Stevens TM, Richards AT, Bewtra C, Sharma P. Tumors metastatic to thyroid neoplasms: a case report and review of the literature. *Patholog Res Int*. 2011;2011:238693. doi: 10.4061/2011/238693.
  15. De Lara S, Parris TZ, Werner Ronnerman E, Helou K, Kovacs A. GATA3 as a putative marker of breast cancer metastasis-A retrospective immunohistochemical study. *Breast J*. 2018;24(2):184-8. doi: 10.1111/tbj.12863.
  16. Sorlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc Natl Acad Sci U S A*. 2001;98(19):10869-74. doi: 10.1073/pnas.191367098.